



# EFFECT OF METHIMAZOLE THERAPY ON THYROID PATHOLOGY THAT MAY MIMIC THYROID MALIGNANCY

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**SUMMARY** – Diffuse toxic goiter, as the most common cause of hyperthyroidism, is usually initially treated with thyrostatic drugs such as methimazole, followed by radioiodine therapy or surgery which may be indicated as definitive treatment. Radioactive iodine therapy has a known association with various histopathologic features including cytologic atypia, but herein we present a rare example of morphological thyrocyte changes induced by long-term pharmacological treatment with methimazole that mimicked thyroid malignancy in a pathohistological sample.

**Key words:** *hyperthyroidism, thyrostatic drugs, thyroid neoplasms*

## Introduction

Diffuse toxic goiter is the most common cause of hyperthyroidism, with an overall prevalence up to 1.3% and clinical symptoms of hypermetabolism and some extrathyroidal manifestations like ophthalmopathy and dermopathy. It is an autoimmune disease caused by interplay of genetic and environmental factors, with higher incidence in women than in men [1]. Therapy includes thyrostatic drugs or radioiodine therapy and surgery if spontaneous remission is not achieved. In the past, the association of radioactive iodine therapy with various histopathologic features including cytologic atypia has been described [2-6]. In this paper, we present a rare example of morphological thyrocyte changes induced with long-term methimazole therapy that mimicked thyroid malignancy in a pathohistological sample.

## Case report

A 67-year-old female patient presented with tremor, palpitations, sweating, and weight loss that lasted for 2 months; laboratory findings indicated high level of total thyroxine and triiodothyronine with suppressed TSH levels. The patient also presented with atrial fibrillation.

Thyroid ultrasound revealed diffuse thyroid goiter that indicated diffuse toxic goiter. Thyrostatic therapy was introduced as a 60 mg dose of methimazole daily for the first 7 days with gradual decrease in 10-day intervals. After 5 weeks, the patient showed good therapy response with normalization of thyroid hormone levels and clinical remission, so maintenance therapy was continued with 10 mg of methimazole daily. Two years later, the patient developed mild to severe ophthalmopathy. Despite suggestions and indications, the patient rejected surgery so methimazole therapy was continued with some relapses and dose adjustment. Four years later, the patient agreed to surgical treatment and total thyroidectomy was per-

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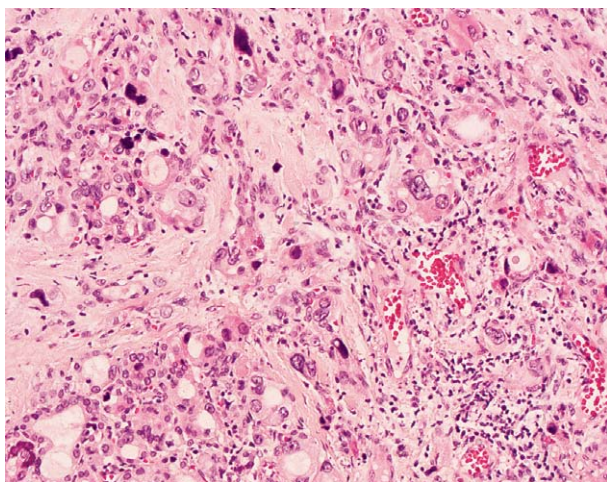


Figure 1a. High-power view showing foci of cytologic atypia (hematoxylin and eosin  $\times 20$ )

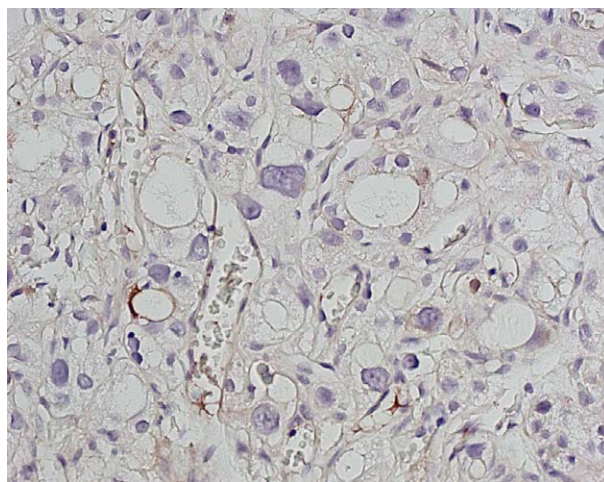


Figure 1c. Lack of Immunoreactivity for CK 19 ( $\times 20$ ).

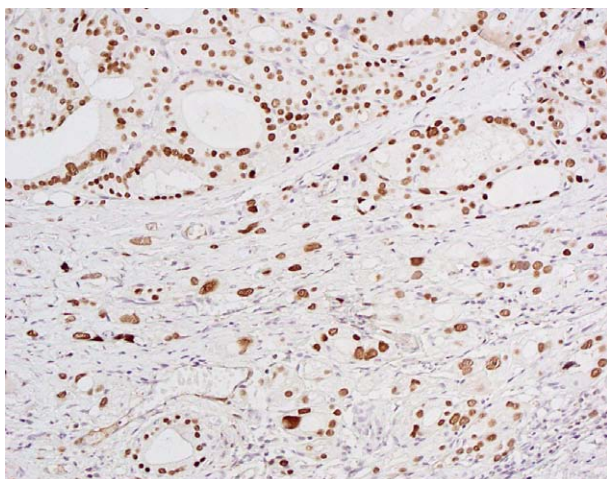


Figure 1b. Diffuse immunoreactivity for TTF-1 ( $\times 20$ ).

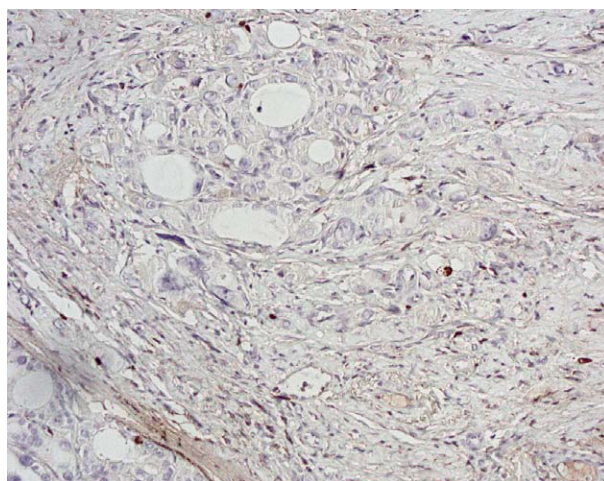


Figure 1d. Low proliferative Ki-67 index ( $\times 20$ ).

formed. At the time of the surgery the patient was receiving a lower dose of 10–15 mg methimazole daily. In the early postoperative period, the patient presented with a complication that consisted of hemorrhage with urgent tracheotomy and 24 h mechanic ventilation and good recovery during next few days.

### Histologic features

Gross features: The left lobe measured 5×4×2 cm in diameter while the right lobe measured 5×4×3 cm. Histologic features: surgically resected thyroid gland showed incomplete regression combined with hyperplastic changes. Thyroid tissue showed pronounced

nodularity accompanied with perinodular fibrosis. The amount of lighter colloid varied in different areas, and epithelial hyperplasia with focal papillary hyperplasia was observed. Psammoma bodies were also present. Follicular cells focally showed marked cellular polymorphism with nuclear atypia and hyperchromasia (Figure 1a). Immunostains revealed cells positive for TTF-1 (Figure 1b), negative for CK 19 (Figure 1c), and with proliferative activity below 5% measured by expression of the Ki-67 proliferative marker (Figure 1d).

### Discussion

Our case report represents rare example of methimazole-induced morphological change in thyroid

cells that may mimic thyroid malignancy on pathohistological examination.

On a histologic basis, differential diagnosis comprised thyroid neoplasia, particularly papillary carcinoma. The morphological differentiation between these two entities, accompanied with clinical history and laboratory tests, posed a great challenge and required detailed analysis to exclude the malignancy [7,8].

**Compliance with Ethical Standards:**

**Funding:** None.

**Conflict of interest:** All the authors declare that they have no conflict of interest. This article does not include any studies with human participants or animals performed by any of the authors.

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## Sažetak

### UČINAK TERAPIJE METIMAZOLOM NA PATOHISTOLOŠKI IZGLED TKIVA ŠTITNJACE KOJI MOŽE OPONAŠATI MALIGNNE PROMJENE

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Difuzna toksična struma, kao najučestaliji uzrok hipertireoze, se uglavnom liječi tireostaticima kao što je metimazol a nakon početne farmakološke terapije, ukoliko ne dođe do spontane remisije bolesti, liječenje se nastavlja primjenom radioaktivnog joda (I-131) ili kirurškim zahvatom.

Primjena radioaktivnog joda dovodi do brojnih histopatoloških izmjena u parenhimu štitnjače, uključujući i staničnu atipiju, no u našem radu prikazujemo rijedak slučaj utjecaja dugotrajne farmakološke terapije metimazolom na izmjenu morfologije tireocita koja može oponašati izgled malignih stanica na histološkom uzorku tkiva štitnjače.

**Ključne riječi:** *hipertireoza, tireostatska terapija, neoplazme štitnjače*